METHYLPHENIDATE EXTENDED RELEASE CHEWABLE TABLET

BACKGROUND OF THE INVENTION

Methylphenidate hydrochloride (HCl) and dexmethylphenidate hydrochloride both have the empirical formula $C_{14}H_{19}NO_2$.HCl. Methylphenidate HCl is a racemic mixture of d,l-threo-methyl α-phenyl-2-piperidineacetate hydrochloride. Several commercial products, including, e.g., Ritalin®, Daytrana™, and Metadate™ contain methylphenidate HCl as the active drug. Dexmethylphenidate is the d-threo-enantiomer of racemic methylphenidate hydrochloride [Focalin® product literature]. There are several commercial products which contain dexmethylphenidate as the active drug.

The use of the central nervous system stimulants methylphenidate and dexmethylphenidate for the treatment of such conditions as attention deficit disorder (ADD) and attention deficit hyperactivity disorder (ADHD) in adults and children has been described [see, Focalin®, Concerta®, Ritalin®, Daytrana™ and Metadate® product literature]. This drug may also be used to treat depression and cognitive impairment following Traumatic Brain Injury [See, product literature for methylphenidate hydrochloride tablet which is commercially available from Lake Erie Medical DBA Quality Care Products LLC, and product literature of the other drug products identified herein].

Solid dose methylphenidate or dexmethylphenidate products are commercially available having an extended release profile of 8 hours according to the product label. These products include, e.g., Ritalin® LA and Methylin® ER tablets have product labels indicating that they must be swallowed whole without crushing or chewing. Liquid methylphenidate dosage forms have also been described which are predominantly designed for children, including children as young as 3 years old who have difficulty swallowing solid dosage forms.

There remains a need for a quick-acting, stable, extended release methylphenidate product which can be conveniently delivered in a form suitable for patients who have difficulty swallowing solid tablets and capsules.

SUMMARY OF THE INVENTION

The present invention provides a methylphenidate extended release chewable tablet which provides a fast onset of MPH and a twelve-hour release profile. The chewable tablet can be divided into portions and these tablet portions retain the fast onset and 12 hour release profile of the intact tablet. In one embodiment, the tablet is scored to facilitate splitting when desired. Methods of treating patients in need thereof with these methylphenidate (MPH) extended release chewable tablets are further provided by the invention.

The MPH extended release chewable tablet comprises (i) two different immediate release methylphenidate components, each of which provides a different immediate release profile, and (ii) about 50% to about 90% w/w of a sustained release barrier coated methylphenidate-ion exchange resin complex-matrix, based on the total weight of the methylphenidate components.

The first immediate release methylphenidate components is an uncoated methylphenidate-ion exchange resin complex, optionally in combination with a matrix forming polymer which is characterized herein as the "slower" onset immediate release component. The second immediate release component is a faster onset immediate release methylphenidate component which is a methylphenidate, pharmaceutically acceptable salt thereof, or hydrate thereof as defined herein, which is not complexed with or bound to an ion exchange resin. The sustained release component has a barrier coating which is a pH-independent release, high tensile strength, water insoluble, water-permeable barrier coating.

In another embodiment, the invention provides a scored chewable tablet, wherein dividing the tablet does not significantly modify the in vitro profile of the tablet portions resulting from split or other division of the intact tablet.

In one embodiment, a methylphenidate extended release chewable tablet comprises methylphenidate components in a combination of (a) about 60% w/w-80% w/w of a sustained release, cured, barrier coated methylphenidate-ion exchange resin complex-matrix, wherein the barrier coating comprises polyvinylacetate and a plasticizer (b) about 10% w/w to about 20% w/w of a combination of an immediate release uncoated methylphenidate-ion exchange resin complex and (c) about 10% w/w to about 20% w/w of an immediate release uncomplexed methylphenidate. Throughout this specification, when weight percentages and/or ratios are provided for methylphenidate in each of the three active components, the weights are based on the amount of methylphenidate base in each component. As used herein the term "uncomplexed methylphenidate" is referred to as the faster onset immediate release component and specifically includes a free base methylphenidate, as well as a pharmacologically active and physiologically compatible salt form thereof, including acid addition salts, and hydrates thereof; specifically excluded from the term "uncomplexed methylphenidate" is a methylphenidate which bound to or complexed with an ion exchange resin.

In a further embodiment, the invention provides a method of treating patients with a disorder for which methylphenidate is regulatory approved by administering a methylphenidate extended release chewable tablet as described herein.

Still other aspects and advantages of the invention will be apparent from the following detailed description of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a linear plot of mean methylphenidate plasma concentration versus time using non-transformed data. This study provides the pharmacokinetic (pK) profile of a single oral chewable tablet formulation of the invention dosed as described in Example 2 to provide an amount of methylphenidate equivalent to a 40 mg dose of methylphenidate HCl. A commercially available immediate release methylphenidate HCl tablet (Methylin® 10 mg chewable tablet, 2×20 mg delivered six hours apart (q6 h)) was used as reference.

DETAILED DESCRIPTION OF THE INVENTION

In one aspect the invention provides a methylphenidate (MPH) extended release chewable tablet. The MPH contains a combination of two different immediate release MPH components and a sustained release MPH component. Suitably, following administration of a single dose of the oral MPH extended release chewable tablet, in some embodiments, a therapeutically effective amount of MPH is reached in less than about thirty minutes, and as soon as about twenty, ten, or fewer minutes, and the formulation provides an extended release profile to at least about 12 hours.